Overview of MGK® Repellent 326
Risk Assessment

May 16, 2003

Introduction

This document summarizes EPA's human health, environmental fate, and ecological risk findings for the pesticide MGK® Repellent 326. These findings are presented fully in the human health risk assessment document *"MGK® Repellent 326 (di-n-propyl isocinchomerate) HED Risk Assessment for Reregistration Eligibility Decision (RED)*" dated April 7, 2003; and the environmental fate and effects risk assessment document, *"MGK 326/Disopropyl isochinomerate (sic) RED"* dated December 24, 2002.

The purpose of this overview is to assist the reader in understanding the conclusions reached in the risk assessments by identifying the key features and findings of each. The overview was developed in response to comments and requests from the public that indicated EPA's risk assessments were difficult to understand, too lengthy, and that it was not easy to compare the assessments for different chemicals due to the use of different formats.

Use Profile

MGK® Repellent 326 is used solely as a component of insect repellent formulations. However, it is never used alone as the sole active ingredient (a.i.), and seldom used as the sole repellent. Rather, it is mostly used to expand the repellency of other formulation components, such as DEET (N,N-diethyl-m-toluamide) or pyrethrins. There are several ready-to-use products formulated in lotions, aerosol or pump sprays, roll-on sticks, gels, creams, shampoos (animals only), and towelettes. These products are applied on an "as needed" basis. The liquid formulated products are used to prepare dip treatments for pets.

- Technical Registrant: McLaughlin Gormley King (MGK) Company is the technical registrant for MGK® Repellent 326 and has provided the primary data for reregistration.

- Annual Poundage: Based on information provided by the technical registrant, from 1997 to 2001, the average total annual domestic usage of MGK® Repellent 326 was approximately 26,000 pounds of a.i. According to the technical registrant, in 2002, 38% of the total amount of MGK® Repellent 326 was sold to customers with pesticide labels for use as "personal insect repellents," 54% for use on horses, and 8% for use on dogs and cats.

- Insect Repellent Uses: Registered products containing MGK® Repellent 326 are intended for application to companion animals (i.e., kittens, cats, puppies, dogs, and horses) and their outdoor premises (i.e., the interior of kennels, barns, etc.). MGK® Repellent 326 products are also intended for direct application to humans.

- Formulations for Use on Humans & Methods of Application: MGK® Repellent 326 is always combined with DEET and MGK 264, with DEET being the primary active ingredient. Aerosol products range from 1.0% to 2.5% active ingredient and labels specify to "apply to cover exposed skin or clothing." The other products for use on humans are lotions or liquids, which range from 1.76% to 4.0% MGK® Repellent 326. The labels for liquid and lotion products direct the user to "apply to cover exposed skin."

- Formulations for Use on Companion Animals & Methods of Application: Formulations for use on companion animals contain many other active ingredients, including several pyrethroids. Products used for dip applications to dogs and cats contain 4.0% MGK® Repellent 326 with the label directing users to dilute at the rate of 1 fl. oz. of product in 1 gallon of water. There are also spray and towelette products with 0.2% and 1.0% active ingredient, respectively, that are applied to horses. The concentrate products contain a maximum of 5.0% active ingredient and the directions are to apply undiluted material with a mist applicator at the rate of 1 fl. oz. per 1000 sq. ft. of space in outdoor premises (i.e., the interior of kennels, barns, etc.).

Human Health Risk Assessment

Dietary Risk from Food

Currently, there are no registered uses involving direct application of MGK® Repellent 326 to agricultural crops or to livestock (including horses) intended for slaughter. Therefore, there are no potential dietary (food) exposures from the use of MGK® Repellent 326, and a dietary (food) risk assessment was not conducted. EPA will propose to revoke all the following established tolerances, found at 40 CFR § 180.143 because the uses have been deleted: meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep, and milk.

Dietary Risk from Drinking Water

Drinking water exposure to pesticides can occur through surface and ground water contamination. Products containing MGK® Repellent 326 are applied as personal and companion animal insect repellents, therefore, its use is not expected to contaminate drinking water.

- Regarding the personal use, the Agency expects the amount of product that is washed off the human body which could contaminate drinking water to be negligible.

- Regarding the companion animal use, products used as surface sprays of premises (e.g., the interior of kennels, barns etc.) should not result in contamination of drinking water. Also, products used as pet dips would be discharged as waste water to septic systems or to sewage treatment plants. Although it is possible that disposed MGK® Repellent 326 could pass on to surface or ground water following treatment, the Agency expects the amount reaching drinking water sources to be negligible, due to the low percentages of MGK® Repellent 326 used in the product formulations.

Residential Risk

Due to limited use patterns of MGK® Repellent 326, this risk assessment was conducted for residential exposure pathways only. Potential residential scenarios include short (1-30 days) and intermediate (1-6 months) term exposures that occur when people apply the product topically to themselves or to pets. The Agency assessed three major exposure scenarios: 1) dermal exposure from direct application of MGK® Repellent 326 to human skin; 2) incidental oral exposure of children from topical application (i.e., incidental hand to mouth contact after repellent is applied to a child's skin, or after transfer of residue from a treated pet to a child's hands); and 3) inhalation exposure from use of repellent sprays.

Non-Cancer Residential Risk Summary

- Non-cancer risk is measured by a Margin of Exposure (MOE) which reflects how close the residential exposure comes to the No Observed Adverse Effect Level (NOAEL) taken from animal studies. The margin of exposure (MOE=NOAEL/exposure) is compared to a target MOE. The target MOE is the same value as the uncertainty factor (UF) applied to the NOAEL from the relevant toxicity study. The traditional uncertainty factor is 100x (10x to account for interspecies extrapolation and 10x to account for intraspecies variations), plus any additional safety factors retained due to other concerns such as to the protection of infants and children under the Food Quality Protection Act (FQPA). A MOE less than the target MOE is typically of concern to the Agency.

- For MGK® Repellent 326, the Agency concluded that an additional FQPA safety factor was not necessary because it is not registered for use in/on foods and has no supported or proposed new tolerances. Although the special FQPA safety factor was not applied to this risk assessment, the Agency examined the toxicity and exposure databases to determine if any special concerns for infants and children exist. Based on this examination, the Agency has determined that this risk assessment is adequately protective of all population subgroups, including infants and children without use of an additional uncertainty factor.

- The NOAELs and Low Observed Adverse Effect Levels (LOAELs) used in the residential risk assessment are summarized below:

    ! Short- and intermediate-term dermal and incidental oral risk assessments from the use of MGK® Repellent 326 are based on a NOAEL of 65 mg/kg/day from a two-generation reproduction study in the rat. Decreased pup body weight occurring on lactation days 14-21 was observed at a LOAEL of 250 mg/kg/day.

- Due to the seasonal use pattern of MGK® Repellent 326, long-term (greater than 6 months) exposure is not expected, therefore, an endpoint dose for long-term exposure was not selected and a risk assessment was not conducted for long-term scenarios.

- Since the dermal exposure endpoints were selected from oral toxicity studies, a dermal absorption factor is required to convert the oral dose to an equivalent dermal dose for the risk assessment. The Agency used a 5% dermal absorption factor, based on 8-hour exposure measures made in the dermal absorption studies conducted with formulated MGK® Repellent 326 in humans.

- The dermal exposure values in this assessment were obtained from the 1990 survey study conducted for the insecticide repellent DEET and submitted by a joint group of registrants, the DEET Joint Venture/Chemical Specialties Manufacturers Association. Based on the DEET survey data, repellent products containing DEET and MGK® Repellent 326 were used on an average of 7.5 times and 60% of the yearly sales occur during the months of June and July, the time period in which the survey was conducted. Therefore, the Agency believes that the DEET survey study provides the most definitive data currently available for estimating exposures to MGK® Repellent 326 from use of insect repellants.

- Inhalation exposure is negligible compared to dermal exposure, particularly when applications are made using non-aerosol products. There would be virtually no vapor generated by non-aerosol products. All MGK® Repellent 326 labels prohibit the spraying of the face, therefore, any inhalation exposure from aerosol applications is expected to be extremely short and yield negligible exposure. As a result, an inhalation exposure assessment was not conducted for MGK® Repellent 326. Thus, dermal exposure is the primary route of exposure for MGK® Repellent 326.

- For MGK® Repellent 326, the target MOE is 100 for all routes (inhalation, dermal, and incidental oral) of exposure. The MOEs estimated for all of the residential exposure scenarios evaluated were greater than 100 (Table 1). Therefore, residential non-cancer risks are not of concern.

Table 1: MGK® Repellent 326 MOEs for Non-Cancer Residential Exposure

Exposure Scenario	MOE [1]	Target MOE
Dermal [2] (All subgroup populations)	270- 770	100
Inhalation	Not required based on lack of vapor pressure and use pattern.	
Incidental Oral (Child ≤ 12 years)	4100	100
Aggregate: Dermal and Incidental Oral Combined (Child ≤ 12 years)	250	100

[1] Assumes one application per day. Children may use up to 3 applications/day and adults up to 8 applications/day without a risk concern.

[2] 5% Dermal Absorption Factor applied.

- Aggregate risk from different residential exposure pathways is estimated for the child exposure scenario only, since the child may be exposed via both the incidental oral and dermal pathways, while the adult exposure is from the dermal route only. The aggregate MOE for the child is calculated by adding exposure estimates from the oral and dermal pathways. The aggregate MOE for the child is 250, which is above the target MOE and, therefore, not of concern (Table 1).

- According to incident reports, no illness cases have been reported due to exposure to MGK® Repellent 326. There have been incidents reported from other active ingredients mixed with MGK® Repellent 326, however, they were not attributed to MGK® Repellent 326.

Cancer Residential Risk Summary

- MGK® Repellent 326 is currently classified as a probable human carcinogen (Group B2), based on findings in both the rat and the mouse studies.

- EPA quantified the cancer risk using a linear low-dose (Q_1*) extrapolation based on male mouse liver adenomas and/or carcinomas. Using the Q_1* of 1.6×10^{-3} $(mg/kg/day)^{-1}$, the estimated residential cancer risk for MGK® Repellent 326 is 5×10^{-6}. In general, the Agency is concerned if cancer risk estimates exceed 1×10^{-6}. Therefore, MGK® Repellent 326 may present potential cancer risks of concern from residential exposure.

- In general, this assessment can be characterized as providing a conservative estimate of risk from exposure to MGK® Repellent 326 based on the following:

    ! Estimates of daily and annual exposures to MGK® Repellent 326 were based on actual amounts applied to both skin and clothing from the 1990 DEET survey data. As part of the assessment it was assumed that the residues from both clothing and skin were absorbed into the skin; however, it is unlikely that the amount applied to clothing is going to be fully absorbed into the skin.

    ! The Q_1* value selected is the 95th percentile on the dose response curve. Coupled with conservative exposure assumptions, the cancer risk estimate represents an upper bound of potential risk.

    ! It is assumed that individuals are exposed annually for a lifetime (i.e., 70 years) for the cancer risk estimate. However, products containing MGK® Repellent 326 may not actually be used every year during a person's lifetime.

- The registrant has indicated that there is a possibility they may conduct voluntary studies to demonstrate a mechanism of action for carcinogenicity. At this time, the registrant has not submitted additional data and there is no record of a pathology peer review group convening to re-evaluate the cancer classification; therefore, this issue has not been revisited by the Agency.

Aggregating Risks from Food, Drinking Water and Residential Exposures

Since there is no potential for concurrent exposure via food, water and residential pathways, an aggregate assessment of risk from these combined pathways was not conducted and aggregate risk is equal to residential risk.

Occupational Risk

There are no specific occupational uses of MGK® Repellent 326. Survey and/or marketing data show that MGK® Repellent 326 is not typically applied on a regular basis by professional pet groomers or veterinarians. Therefore, based on current use patterns, only residential exposure pathways were included in the MGK® Repellent 326 risk assessment.

Cumulative Risk and Endocrine Disruptor Effects

Risks summarized in this document are those that result only from the use of MGK® Repellent 326. The Food Quality Protection Act (FQPA) requires that the Agency consider "available information" concerning the cumulative effects of a particular pesticide's residues and "other substances that have a common mechanism of toxicity." The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually.

The Agency has not yet initiated a review to determine if there are any other chemical substances that have a common mechanism of toxicity with that of MGK® Repellent 326. Therefore, for purposes of reregistration, the Agency assumes that MGK® Repellent 326 does not have a common mechanism of toxicity with other substances. However, it is important to note that MGK® Repellent 326 is an organophosphonate as opposed to an organophosphate. MGK® Repellent 326 is structurally different from, has a different toxicological profile, and exhibits different physical/chemical properties than traditional organophosphate compounds.

The Agency is in the process of developing criteria for characterizing and testing endocrine disrupting chemicals and plans to implement an Endocrine Disruptor Screening Program. MGK® Repellent 326 will be reevaluated at that time and additional testing may be required. The available toxicity data show no evidence of endocrine disruption.

Ecological Risk

Based on current use patterns and relatively low toxicity of MGK® Repellent 326, risks to nontarget organisms, including endangered species, are not anticipated; therefore no ecological risk assessments was conducted.

Summary of Pending Data Requirements

All pertinent data requirements for reregistration of MGK® Repellent 326 are satisfied, except for the following outstanding guideline studies:

830.1700 Preliminary Analysis
830.1750 Certified Limits
830.1800 Enforcement Analytical Method
830.7050 UV/Visible Absorption

These studies are not expected to alter the conclusions of this risk assessment.